PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 07 November 2000 (07.11.00)	
International application No. PCT/US00/05158	**Applicant's or agent's file reference** 1046-PCT-00
International filing date (day/month/year) 01 March 2000 (01.03.00)	**Priority date** (day/month/year) 01 March 1999 (01.03.99)
Applicant BECKER, Jeffrey, M. et al	

1. The designated Office is hereby notified of its election made:

   [X] in the demand filed with the International Preliminary Examining Authority on:

   06 September 2000 (06.09.00)

   [ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

   [ ] was not

   made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Zakaria EL KHODARY
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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8 September 2000 (08.09.2000)

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WO 00/52162 A3

(51) International Patent Classification[7]: C12N 15/12, C07K 14/705, 14/70, A01N 33/00, C12N 15/82, A01H 5/00

(21) International Application Number: PCT/US00/05158

(22) International Filing Date: 1 March 2000 (01.03.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/122,312 1 March 1999 (01.03.1999) US

(71) Applicant *(for all designated States except US)*: **THE UNIVERSITY OF TENNESSEE RESEARCH CORPORATION** [US/US]; Suite 403, 1534 White Avenue, Knoxville, TN 37996-1527 (US).

(71) Applicants and
(72) Inventors: **BECKER, Jeffrey, M.** [US/US]; 7125 Cresthill Drive, Knoxville, TN 37919 (US). **HAUSER, Melinda** [US/US]; 10000 Shady View Lane, Knoxville, TN 37922 (US). **DONHARDT, Amy** [US/US]; Apartment 154, 6010 Sunbeam Lane, Knoxville, TN 37920 (US). **BARNES, David** [US/US]; 1540-A Visalia Avenue, Berkeley, CA 94707 (US).

(74) Agents: **WEISER, Gerard, J.** et al.; Schnader Harrison Segal & Lewis LLP, 36th floor, 1600 Market Street, Philadelphia, PA 19103 (US).

(81) Designated States *(national)*: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*

(88) Date of publication of the international search report:
4 January 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 00/52162 A3

(54) Title: EUKARYOTIC PEPTIDE UPTAKE SYSTEM FOR TRANSPORTATION OF ENKEPHALINS

(57) Abstract: An oligopeptide transporter in the yeast *Saccharomyces cerevisiae* mediates the uptake of tetra- and pentapeptides, including the endogenous opioids leucine enkephalin (Tyr-Gly-Gly-Phe-Leu) and methionine enkephalin (Tyr-Gly-Gly-Phe-Met). The transporter is encoded by the gene OPT1. The system is specific for tetra- and pentapeptides and can be inhibited by the opioid receptor antagonists naloxone and naltrexone. Vectors allowing expression of OPT1 and methods of use are disclosed. Treatment of OPT1p with toxic enkephalins as an antifungal method is also disclosed.

PATENT COOPERATION TREA

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
1046-PCT-00		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 00/ 05158	01/03/2000	01/03/1999
Applicant		
THE UNIVERSITY OF TENNESSEE RESEARCH CORPORATION		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [X] furnished subsequently to this Authority in written form.

   [X] furnished subsequently to this Authority in computer readble form.

   [X] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [X] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [X] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/05158

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/12 C07K14/705 C07K14/70 A01N33/00 C12N15/82 A01H5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K A01N A01H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
BIOSIS, EPO-Internal, FSTA, MEDLINE, STRAND, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LUBKOWITZ MARK A ET AL: "Schizosaccharomyces pombe isp4 encodes a transporter representing a novel family of oligopeptide transporters." MOLECULAR MICROBIOLOGY, vol. 28, no. 4, May 1998 (1998-05), pages 729-741, XP000929697 ISSN: 0950-382X cited in the application the whole document	1-18
A	WO 98 34950 A (UNIV TENNESSEE RES CORP ;BECKER JEFFREY M (US); LUBKOWITZ MARK A () 13 August 1998 (1998-08-13) the whole document	1-18

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 August 2000	07/09/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Lejeune, R

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	LUBKOWITZ MARK A ET AL: "An oligopeptide transport gene from Candida albicans." MICROBIOLOGY (READING), vol. 143, no. 2, 1997, pages 387-396, XP000929716 ISSN: 1350-0872 the whole document ---	1-18
P,X	HAUSER M ET AL: "Enkephalins are transported by a novel eukaryotic peptide uptake system." JOURNAL OF BIOLOGICAL CHEMISTRY., vol. 275, no. 5, 4 February 2000 (2000-02-04), pages 3037-3041, XP002144948 AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD., US ISSN: 0021-9258 the whole document ---	1-3, 15-18
A	TYNKKYNEN S ET AL: "Genetic and biochemical characterization of the oligopeptide transport system of Lactococcus lactis." JOURNAL OF BACTERIOLOGY 1993 RES. & DEV. CENT., VALIO LTD., PO BOX 390, SF-00101 HELSINKI, FINLAND, vol. 175, no. 23, pages 7523-7532, XP000929851 the whole document -----	1

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/05158

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9834950 A	13-08-1998	EP 1015482 A	05-07-2000

PATENT COOPERATION TREATY

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REC'D 17 JUL 2001
WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
1046-PCT-00		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/05158	01 MARCH 2000	01 MARCH 1999
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant THE UNIVERSITY OF TENNESSEE RESEARCH CORPORATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☒ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06 SEPTEMBER 2000	27 JUNE 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer BRONWEN M. LOEB Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/05158

I. Basis f the report

1. With regard to the elements of the international application:*

[X] the international application as originally filed

[X] the description:
pages (See Attached) , as originally filed
pages , filed with the demand
pages , filed with the letter of

[X] the claims:
pages (See Attached) , as originally filed
pages , as amended (together with any statement) under Article 19
pages , filed with the demand
pages , filed with the letter of

[X] the drawings:
pages (See Attached) , as originally filed
pages , filed with the demand
pages , filed with the letter of

[X] the sequence listing part of the description:
pages (See Attached) , as originally filed
pages , filed with the demand
pages , filed with the letter of

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/05158

II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

   ☐ copy of the earlier application whose priority has been claimed.

   ☐ translation of the earlier application whose priority has been claimed.

2. ☒ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

The priority document does not provide an enabling disclosure or written description for the claims as filed.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/05158

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additi nal fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1.

Group I, claim(s)1-3, 15-18, drawn to a method for obtaining mammalian enkephalin transport proteins using expression in yeast.
Group II, claim(s) 4-9, drawn to an antifungal composition and a method of using it.
Group III, claim(s) 10-14, drawn to a vector for transformation of plant cells and a method of using it.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Each group has a different special technical feature not shared by the remaining groups. Group I is drawn to a method for obtaining mammalian enkephalin transport proteins. Group II is directed to an antifungal composition, and a method to use it, which has the special technical feature of using a toxic derivative of enkephalins as an active ingredient. Group III is directed to a vector for transformation of plant cells and a method of using it, which has the special technical feature of comprising a nucleic acid molecules encoding the protein of SEQ ID NO. 2.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. _.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/05158

V. Reasoned statement und r Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such stat ment

1. statement

Novelty (N)	**Claims**	1-18	**YES**
	Claims	NONE	**NO**
Inventive Step (IS)	**Claims**	NONE	**YES**
	Claims	1-18	**NO**
Industrial Applicability (IA)	**Claims**	1-18	**YES**
	Claims	NONE	**NO**

2. citations and explanations (Rule 70.7)

Claims 1-18 are directed to a method for obtaining mammalian enkephalin transport proteins, an antifungal composition, a method of reducing or preventing fungal growth, a vector for transformation of plant cells, transformed cells and a method for cultivating plant material. These inventions were neither described nor enabled in the priority application. Therefore, claims 1-18 are being examined in light of the internation filing date of 01 March 2000.

Claims 1-3 and 15-18 lack an inventive step under PCT Article 33(3) as being obvious over Hauser et al. Hauser et al teach that the product of the yeast OPT1 gene can mediate enkephalin uptake (entire document). Hauser et al suggest the use of the yeast OPT1 gene in finding mammalian homologs (Abstract and p. 3040, final sentence). Cloning methods for mammalian genes are well-known to one of ordinary skill in the art. One of ordinary skill in the art would be motivated to use well-known cloning methods to obtain a mammalian enkephalin transport protein because of its clear medical value.

Claims 4-9 lack an inventive step under PCT Article 33(3) as being obvious over Rolka et al in view of Hauser et al, Univ. Tennessee Res. Corp. (WO 98/34950) and Andruskiewicz et al. Rolka et al teach toxic enkephalin analogs containing toxic amino acids (entire document). Hauser et al teach that yeast OPT1 gene product mediates uptake of enkephalins (entire document). Hauser et al further teach that the yeast OPT1 gene is a member of the OPT family of peptide transporters which family also includes Candida albicans (p. 3037, Introduction). Andruszkiewicz et al teach pentapeptides containing N3-(4-methoxyfumaroyl)-L-2,3-diaminopropanoic acid, have antifungal properties (p. 133, Table III). It would be obvious to one of ordinary skill in the art to combine the teachings of Rolka et al, Hauser et al, Andruszkiewicz et al to make an antifungal composition comprising a toxic derivative enkephalin. One would be motivated to do so because Univ. Tennesse Res. Corp. et al suggest it (Abstract and pages 4-5). The choice of toxic derivative would be obvious to (Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/05158

VII. Certain defects in the international application

The following defects in the form or contents f the international applicati n have been noted:

Claim 13 objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: it ends with two periods.

No page 16 was included in the draawings and has been treated accordingly.

VIII. Certain bservations on th international application

The following observations on the clarity of the claims, descripti n, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 6, 7 and 15-18 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): Claim 6 uses the terms "mutagenic nucleotide analogues" and "mutagenic nucleoside analogues" however the description does not define what these are. Claim 7 uses the term "unusual D-amino acids" which is vague and indefinite as the modifier "unusual" has no precise meaning and the description does not define it. Claims 15-18 are vague and indefinite as they lack a step which clearly relates back to the preamble.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:
The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): C12N 15/12, 15/82; C07K 14/705, 14/70; A01N 33/00; A01H 5/00 and US Cl.: 435/320.1,419,420,440; 514/2; 530/302

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
page(s) 1-34, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
page(s) 35-38, as originally filed.
page(s) NONE, as amended under Article 19.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the drawings,
page(s) 1-15,18-21, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the sequence listing part of the description:
page(s) NONE, as originally filed.
pages(s) NONE, filed with the demand.
and additional amendments:
NONE

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
one of ordinary skill in the art.

Claims 10-14 lack an inventive step under PCT Article 33(3) as being obvious over Hauser et al in view of Becker et al and West et al. Hauser et al teach that yeast OPT1 gene product mediates uptake of enkephalins (entire document). Hauser et al further teach that the yeast OPT1 gene is a member of the OPT family of peptide transporters which family also includes Candida albicans (p. 3037, Introduction). Univ. Tennessee Res. Corp. teach the idea of using OPT genes in plant cells in order to use specific oligopeptides as growth stimulators (page 5). It would be obvious to one of ordinary skill in the art to combine these teachings to develop a method of cultivating plant material using a vector for transforming plant cells comprising an OPT1 gene. One would be motivated to do so as it is well known that endogenous peptide transport is a significant source of nutrition. See for instance West et al, page 21, Abstract. The choice of plant to transform is obvious to one of ordinary skill in the art and one would be motivated to do so by the commercial demands of agriculture and horticulture.

---------- NEW CITATIONS ----------

ANDRUSZKIEWICZ et al. Anticandidal properties of N3-(4-methoxyfumaroyl)-L-2,3,-diaminopropanoic acid oligopeptides. J. Med. Chem. 1990, Vol. 33, pages 132-135.

ROLKA et al. Opiate-like peptides. Part XII. Synthesis and some biological properties of met-enkephalin analogues modified in position 2 by D-alanyl residue in positions 2 and 4 by 3-(2-napthyl)-D-alanyl residue. Pol. J. Pharmacol. Pharm. 1989, Vol. 41, pages 147-155.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

WEST et al. Cloning and functional characterisation of a peptide transporter expressed in a the scutellum of barley grain during the early stages of germination. The Plant Journal. 1998, Vol. 15, pages 221-229.